Claims

1. Viral vector, characterized in that it compris s an expression unit containing one or mor viral gen s; said expression unit being functional in a complementation cell and nonfunctional in a host cell, and comprising one or more heterologous regulator sequence(s).

2. Viral vector according to claim 1, characterized in that said expression unit comprises one or more regulatory sequence(s) enabling to activate the expression of said viral gene in the presence of an inducer and/or to inhibit the expression of said viral gene in the presence of a repressor.

3. Viral vector according to claim 1 or 2, characterized in that said regulatory sequence can act at the level of transcription, elongation, transport or stability of the messenger RNAs or translation.

4. Viral vector according to claim 3, characterized in that said regulatory sequence is placed at the level of the promoter of said unit, and more especially upstream of the TATA box.

5. Viral vector according to one of Claims 1 to 4, characterized in that said expression unit comprises one or more regulatory sequence(s) selected from the TAR, RRE, GRE, PRE, ERE and Gal4 UAS sequences and the regulatory sequences of the metallothionein gene and of the bacterial tryptophans lactose and tetracycline operons.

6. Viral vector according to claim 5, characterized in that said expression unit comprises one or more regulatory sequence(s) derived from the tetracycline operon, placed upstream of the TATA box of said promoter, to give a promoter which is activable by an inducer of the tetracycline transactivator (tTA) type and repressible by tetracycline.

7. Viral vector according to claim 5, characterized in that said expression unit comprises one or more regulatory sequence(s) derived from the tetracycline operon, placed downstream of the TATA box of said promoter, to give a promoter which is r pressible by the tetracycline repressor (T tR).

8. Viral vector according to one of claims 1 to 7, derived from a virus selected from the herpesvirus, cytomegalovirus, AAV (adeno-associated virus), poxvirus and adenovirus.

9. Adenoviral vector according to claim 8, derived from an adenovirus of human, canine, avian, bovine, murine, ovine, porcine or simian origin, or alternatively from a hybrid comprising adenoviral genome fragments of different origins.

10. Viral vector according to claim 8 or 9, characterized in that it is defective for replication.

11. Adenoviral vector according to claim 10, characterized in that it lacks at least all or part of the E1 region and, optionally, all or part of the E3 region.

12. Adenoviral vector according to one of claims 9 to 11, characterized in that it comprises one or more expression unit(s) containing one or more viral genes of the E2, E4 or L1-L5 regions.

13. Adenoviral vector according to claim 12, characterized in that it comprises an expression unit containing one or more regulatory sequence(s) derived from the tetracycline operon, placed upstream of the TATA box of the promoter and open reading frames (ORFs) 6 and 7 of the E4 region, so that the expression of said reading frames is activable by an inducer of the tetracycline transactivator (tTA) type and repressible by tetracycline.

14. Viral vector according to one of claims 1 to 13, characterized in that it comprises an exogenous nucleotide sequence placed under the control of the elements needed for its expression in the host cell.

15. Viral vector according to claim 14, characterized in that the exogenous nucleotide sequence is selected from the genes coding for a cytokine, a cell or nuclear receptor, a ligand, a coagulation factor, the CFTR protein, insulin, dystrophin, a growth hormone, an enzyme, an enzyme inhibitor, a polypeptide having an antitumor effect, a polypeptide capable of inhibiting a bacterial, parasitic or viral infection, and in

particular HIV, an antibody, a toxin, an immunotoxin and a marker.

16. Infectious viral particle comprising a viral vector according to one of claims 1 to 15.

17. Eukaryotic host cell comprising a viral vector according to one of claims 1 to 15 or an infectious viral particle according to claim 16.

18. Complementation cell, characterized in that it comprises an inducer and/or a repressor.

19. Complementation cell according to claim 18, characterized in that it comprises a DNA fragment coding for an inducer and/or a repressor.

20. Complementation cell according to claim 18 or 19, characterized in that it is derived from line 293.

21. Complementation cell according to one of claims 18 to 20, for the complementation of an adenoviral vector which is defective for the E1 function and at least one second, late or early adenoviral function, characterized in that it comprises:

(i) a first cassette for the expression of all or part of the E1 region of an adenovirus, placed under the control of the elements necessary for its expression in said complementation cell, and

(ii) a second cassette for the expression of all or part of a late or early region of an adenovirus other than the E1 region, placed under the control of the elements necessary for its expression in said complementation cell, said elements comprising one or more regulatory sequences according to claims 5 to 7.

22. Complementation cell according to claim 21, characterized in that said elements of the second expression cassette comprise a minimal promoter equipped at its 5′ end with 1 to 20 tet O sequences.

23. Complementation cell according to claim 22, characterized in that said elements of the second expression cassette comprise a minimal promoter derived from the CMV virus (cytomegalovirus) equipped at its 5′ end with 7 tet O sequences.

24. Complementation cell according to one of claims 18 to 23 for the complementation of an adenoviral vector which is defective for the E1 and E4 functions, characterized in that the second expression cassette is a cassette for the expression of all or part of the E4 region of an adenovirus.

25. Complementation cell according to claim 24, characterized in that said second expression cassette is a cassette for the expression of the sequences coding for open reading frames 6 and 7 (ORFs 6/7) of the E4 region of an adenovirus.

26. Complementation cell according to one of claims 18 to 23 for the complementation of an adenoviral vector which is defective for the E1 and E2 functions, characterized in that said second expression cassette is a cassette for the expression of all or part of the E2 region of an adenovirus.

27. Complementation cell according to claim 26, characterized in that said second expression cassette is a cassette for the expression of the sequences coding for the DBP protein (DNA binding protein) of the E2 region of an adenovirus.

28. Complementation cell according to claim 26, characterized in that said second expression cassette is a cassette for the expression of the sequences coding for a temperature-sensitive mutant of the DBP protein of the E2 region of an adenovirus.

29. Complementation cell according to one of claims 18 to 28 for the complementation of an adenoviral vector which is defective for the E1 function and at least two other, late or early adneoviral functions, characterized in that it comprises, in addition, a third cassette for the expression of all or part of a late or early region of an adenovirus other than the E1 region and the adenoviral region of the second expression cassette, placed under the control of the elements necessary for its expression in said complementation cell, and preferably of a promoter as defined in claim 5, 6 or 7.

30. Complementation cell according to claim 29 for

the complementation of an adenoviral vector which is defective for the E1, E2 and E4 functions, comprising:

(i) a first cassette for the expression of all or part of the E1 region of an adenovirus, placed under the control of the elements necessary for its expression in said complementation cell,

(ii) a second cassette for the expression of all or part of the E4 region of an adenovirus, placed under the control of the elements necessary for its expression in said complementation cell, and

(iii) a third cassette for the expression of all or part of the E2 region of an adenovirus, placed under the control of the elements necessary for its expression in said complementation cell,

said elements of the second and/or third expression cassette comprising a promoter equipped with at least one tet O sequence, and more especially a minimal promoter derived from the CMV virus (cytomegalovirus), equipped at its 5' end with 7 tet O sequences.

31. Complementation cell according to one of claims 18 to 30, characterized in that the titer of viral particles produced by said complementation cell is greater than 5×10^8 pfu (plaque forming units)/ml.

32. Complementation cell according to one of claims 18 to 31, characterized in that the titer of viral particles produced by said complementation cell is greater than 1×10^{10} ifu (infectious units)/ml.

33. Method of preparation of an infectious viral particle according to claim 16, according to which:

(i) a viral vector according to one of claims 1 to 15 is introduced into a complementation cell capable of complementing *in trans* said viral vector, to obtain a transfected complementation cell;

(ii) said transfected complementation cell is cultured under suitable conditions to permit the expression of the viral genes and the production of said infectious viral particle; and

(iii) said infectious viral particle is recovered in the cell culture.

34. Method according to claim 33, characterized in that said viral vector is an adenoviral vector and said complementation cell is according to claim 20.

35. Method of preparation of an infectious adenoviral particle, according to which:

(i) an adenoviral vector is introduced into a complementation cell according to one of claims 21 to 32, to obtain an infected complementation cell,

(ii) said transfected [sic] complementation cell is cultured under suitable conditions to permit the expression of the viral genes and the production of said infectious viral particle; and

(iii) said infectious viral particle is recovered in the cell culture.

36. Pharmaceutical composition comprising a viral vector according to one of claims 1 to 15, an infectious viral particle according to claim 16 or obtained employing a preparation method according to one of claims 33 to 35, a eukaryotic host cell according to claim 17 or a complementation cell according to one of claims 18 to 32, in combination with a vehicle which is acceptable from a pharmaceutical standpoint.

37. Therapeutic or prophylactic use of a viral vector according to one of claims 1 to 15, of an infectious viral particle according to claim 16 or obtained employing a preparation method according to one of claims 33 to 35, of a eukaryotic host cell according to claim 17 or of a complementation cell according to one of claims 18 to 32, for the preparation of a medicinal product intended for the treatment of the human or animal body by gene therapy.

38. Use according to claim 37, in combination with a repressor.